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Effect of Low-Fat vs. Other Diet Interventions on Long-Term Weight Change in Adults: A Systematic Review and Meta-Analysis

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Abstract

Background—The effectiveness of low-fat diets for long-term weight loss has been debated for decades, with dozens of randomized trials (RCTs) and recent reviews giving mixed results.

Methods—We conducted a random effects meta-analysis of RCTs to estimate the long-term effect of low-fat vs. higher fat dietary interventions on weight loss. Our search included RCTs conducted in adult populations reporting weight change outcomes at ≥1 year, comparing low-fat with higher fat interventions, published through July 2014. The primary outcome measure was mean difference in weight change between interventions.

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Conflicts of interest statement
Drs. Tobias, Chen, Manson, and Willett have no disclosures.

Author contributions
Dr. Tobias developed the study protocol, conducted the literature search, data extraction, analysis, and interpretation, and draft manuscript. Dr. Chen conducted the literature search, and data extraction. Drs. Manson, Ludwig, Willett, and Hu contributed to study protocol and key data interpretation and manuscript review.

Findings—Fifty-three studies met inclusion criteria representing 68,128 participants. In the setting of weight loss trials, low-carbohydrate interventions led to significantly greater weight loss than low-fat interventions (n comparisons=18; weighted mean difference [WMD]=1.15 kg, 95% CI=0.52 to 1.79; I^2=10%). Low-fat did not lead to differences in weight change compared with other moderate fat weight loss interventions (n=19; WMD=0.36, 95% CI=-0.66 to 1.37; I^2=82%), and were superior only when compared with "usual diet" (n=8; WMD=-5.41, 95% CI=-7.29 to −3.54; I^2=68%). Similarly, non-weight loss trials and weight maintenance trials, for which there were no low-carbohydrate comparisons, had similar effects for low-fat vs moderate fat interventions, and were superior compared with "usual diet". Weight loss trials achieving a greater difference in fat intake at follow-up significantly favored the higher fat dietary interventions, as indicated by difference of ≥5% of calories from fat (n=18; WMD=1.04, 95% CI=0.06 to 2.03; I^2=78%) or by difference in change serum triglycerides of ≥5 mg/dL (n=17; WMD=1.38, 95% CI=0.50 to 2.25; I^2=62%).

Interpretation—These findings suggest that the long-term effect of low-fat diets on body weight depends on the intensity of intervention in the comparison group. When compared to dietary interventions of similar intensity, evidence from RCTs does not support low-fat diets over other dietary interventions.

Introduction

Identifying effective strategies for long-term weight control will be critical to reduce the alarming prevalence of overweight and obesity worldwide. The macronutrient composition of the diet, or the proportions of calories contributed by fat, carbohydrate, and protein, has received significant attention in past decades for its potential relevance in weight loss and weight maintenance. Numerous short- and long-term randomized trials across a variety of general and clinical populations have attempted to identify the optimal ratio of macronutrients for weight loss. Lowering the proportion of daily calories consumed from total fat has been targeted for many reasons, one of which is that a single gram of fat contains more than twice the calories of a gram of carbohydrates or protein (9 kcal/gram vs. 4 kcal/gram). Thus, reducing total fat intake may theoretically lead to an appreciable impact on total calories consumed. However, randomized trials have failed to consistently demonstrate that reducing the percent of energy from total fat leads to long-term weight loss compared to other dietary interventions.

This systematic review and meta-analysis aimed to summarize the large body of evidence from randomized control trials (RCTs) lasting ≥1 year in which weight changes on low-fat diets vs. other dietary intervention groups were compared. Trials were included regardless of whether weight loss was intended or not, for example in studies evaluating lipids or cancer endpoints. We considered stratification by characteristics of the interventions that may affect differences in weight loss, including whether the intervention arms received similar attention and intervention intensity, or the composition of the comparison diet. We hypothesized that low-fat diets would not be associated with greater weight loss when differences in these intervention characteristics were taken into account, and that differences in weight loss favoring higher fat interventions would be larger when adherence was greater.

Methods

Search strategy and inclusion criteria

Predefined search strategy, study eligibility criteria, and statistical methodological approaches, were detailed in our unpublished research protocol. Full details of our literature search (Page 2) and PRISMA checklist (Pages 7–10) are outlined in the Appendix. Briefly, we used the MEDLINE, EMBASE, CENTRAL, and Cochrane Database of Systematic Reviews to identify eligible trials. We included trials lasting ≥1 year comparing weight change on a low-fat diet (as defined by authors) with any higher fat dietary intervention, including "usual diet" among non-pregnant adults. Trials of shorter duration were excluded because weight-loss trials frequently observe an initial maximal weight loss around 6 months with subsequent weight regain.

The outcome of interest was long-term (≥1 year) change in body weight (reported as mean change from baseline, mean change difference, or mean body weight at end of follow-up). Efforts were made to contact authors to obtain variance measures, if not reported, but were ultimately excluded if unavailable. We excluded trials if one intervention group included a non-dietary weight loss component (e.g., exercise regimen, pharmaceutical intervention) while the other did not. We did not make exclusions based on concomitant dietary components (e.g., increase fruits and vegetables). Nonrandomized trials were excluded as well as dietary supplements or meal replacement drink interventions as these were beyond the scope of our investigation. If trial results were published more than once, the paper with the most complete follow-up was included in the main analysis. Screening of abstracts for relevance was conducted by two reviewers (DT, MC) and eligible full texts were reviewed with an inclusion/exclusion criteria sheet independently and in duplicate by two reviewers (DT, MC).

Data extraction

Variables captured from the final accepted studies included study level information (authors, country, center), study population characteristics, intervention details, including weight loss intention (yes, no, maintain) and the relative intensity of each intervention, as described by study authors (i.e., systematically greater attention, time spent with study clinicians, dieticians, program materials, etc for one intervention group over the other), and outcomes by treatment arm. We also recorded dietary adherence, including change in serum triglyceride levels and the percent calories from fat during follow-up. We analyzed the intention-to-treat estimates, when reported.

We evaluated the trials' potential for bias using the Cochrane risk of bias assessment tool.(1) Data were extracted independently by two investigators (DT, MC), and discrepancies resolved with a third reviewer (FH), if necessary.

Data analysis

We calculated the mean difference in body weight change from baseline by subtracting the mean change of the comparison diet group from the mean change in the low-fat diet group. If the mean change was not reported we compared the groups' final mean body weights, under the assumption that randomization resulted in similar average baseline body weights between treatment arms. We estimated the pooled weighted mean difference and 95% confidence interval (CI) with a DerSimonian and Laird random effects model. $P<0.05$ was considered statistically significant.

We assessed heterogeneity from the Mantel-Haenszel model and I^2 values (the percent of variance in the pooled estimate due to between-study differences), with $I^2>50\%$ indicating moderate heterogeneity.(2) Analyses established *a priori* were conducted to evaluate potential heterogeneity by the whether the trial was designed with the intention of weight loss, the composition of the comparison diet (low-carbohydrate, other moderate fat/"healthful" diet, or usual diet), the interventions' relative intensity, , whether either, neither, or both of the interventions included caloric restriction, and the baseline health status of the participants. Additionally, we stratified by change in triglyceride levels and in attained self-reported percent calories from fat, with an increase in triglycerides reflecting a relative decrease in fat intake.(3)

Finally, we conducted sensitivity analyses to assess the robustness of findings. We evaluated the impact of removing the largest study or studies, based on their percent weight in the pooled estimates and restricted to trials conducting intention-to-treat analyses and with ≥100 participants. Primary analyses were repeated using an inverse variance weighted fixed effect model. The Begg (4) and Egger (5, 6) tests were conducted to test for the potential of publication bias by plotting the inverse of the variance against the treatment effect. Analyses were performed using STATA® version 13.1.

Role of the funding source

The funding sources did not participate in the design or conduct of the study; collection, management, analysis or interpretation of the data; preparation, review, or approval of the manuscript. DT had full access to all of the data and the final responsibility to submit for publication.

RESULTS

Our search yielded 3,517 citations (Figure 1), of which 53 RCTs were eligible for inclusion in our analysis (Table 1). The majority of trials were conducted in North America (n=37) and were 1 year in duration (n=27). Twenty trials specifically enrolled participants with prevalent chronic diseases, including breast cancer,(7–10) hypercholesterolemia,(11–13) and type 2 diabetes.(14–22) In addition to 35 weight loss trials, there were 13 trials with no intended intervention on weight, (7–10, 12, 13, 22–28) and 5 weight maintenance trials designed to maintain baseline body weight. (11, 29–32)

The low-fat dietary interventions ranged from very low-fat ≤10% of calories from fat, to more moderate goals of ≤30% of calories from fat. Comparator diets of higher fat intake were diverse, ranging from a single baseline interaction with instructions to maintain "usual diet", to a variety of other dietary interventions, including low-carbohydrate and other moderate-to-high-fat diets. The intensity of the interventions varied from pamphlets or instructions given at baseline only, to multicomponent programs integrating counseling sessions, regular meetings with dieticians, food diaries, cooking lessons, etc., to feeding studies, in which participants were given a significant portion of their food. Caloric restriction was a component of many weight loss interventions, but not all. For example, despite being a weight loss intervention, a low-carbohydrate Atkins-style diet is often *ad libitum* (i.e., eat until satiated).

Our primary meta-analysis included 68,128 adults from eligible randomized clinical trials, reporting a mean weight loss of 2.71 kg (SD=2.8) after a median of 1 year of follow-up, and 3.75 kg (SD=2.7) among weight loss trials. Figure 2 presents the overall results according to weight loss trial design (yes, no, or maintain) and composition of comparator intervention (low-carbohydrate, other higher fat intervention, or usual diet). No difference between low-fat and higher fat dietary interventions was observed when all weight loss trials were combined, although there was significant between-study heterogeneity. Low-carbohydrate weight loss interventions led to an average 1.15 kg greater long-term weight loss than low-fat weight loss interventions, with minimal between-study heterogeneity. No difference, however, was observed between low-fat and other higher fat dietary interventions. Compared with groups only following their usual diet, low-fat weight loss interventions led to 5.41 kg greater weight loss. Non-weight loss trials and weight maintenance trials also found a significant but smaller magnitude of weight loss in low-fat interventions when compared with usual diet, and no difference between low-fat and other higher fat dietary interventions. No long-term non-weight loss or weight maintenance trials compared low-fat with low-carbohydrate dietary interventions.

Table 2 presents analyses stratified by additional trial characteristics, limited to trials of similar intensity to minimize bias from one group receiving more attention and higher intervention intensity. Only 4 of the 17 comparisons among trials without a weight loss goal (13, 22, 24) and 1 of the 6 comparisons among weight maintenance trials (31) remained, limiting our ability to stratify further; thus, Table 2 includes weight loss trials only, which trended towards greater weight loss for higher fat interventions. Stratifying by caloric restriction indicated no significant difference in weight loss between low-fat and higher fat dietary weight loss interventions when interventions were concordant for caloric restriction. Calorie-restricted low-fat diets, however, fared significantly worse compared with non-calorie restricted higher fat interventions. Results were similar for weight loss trials among participants with or without a specific chronic disease at baseline (e.g., breast cancer).

When groups differed by >5% calories from fat at follow-up, higher fat led to significantly greater weight loss than low-fat weight loss interventions. Similarly, weight loss trials with a ≥5 mg/dL greater change in triglycerides for low-fat vs. higher fat interventions, led to significantly greater weight loss for the higher fat groups.

Excluding the Women's Health Initiative trial (96.90% of weight) from weight maintenance trials, did not impact findings (n=5; WMD=-0.77 kg, 95% CI=-1.50 to −0.04, p=0.039; I^2=0.0%, p-heterogeneity=0.95). Results were similar when restricted studies conducting to intention-to-treat analyses (Appendix pages 3–4) and when excluding smaller trials of <100 total participants, although few non-weight loss or weight maintenance trials remained eligible according to these criteria. The fixed effect meta-analysis (Appendix pages 5–6), which gives less weight to smaller trials with greater variance, estimated 0.44 kg greater weight loss for the comparator vs. low-fat interventions among the weight loss trials. Fixed effect analyses stratified by comparator group also indicated greater weight loss for “other higher fat interventions” vs. low-fat in trials with and without a weight loss goal, which showed no difference in the random effects analysis.

Results from the Cochrane risk of bias assessment tool (Appendix pages 10–12) were variable and evaluation was limited for many studies by a lack of reporting. Incomplete outcome data was a high potential source of bias for 39 trials due to dropout and lost-to-follow-up rates exceeding 5%. Differential intervention intensity was deemed a source of bias for 20 trials. Both the Begg and Egger’s tests for small-study effects did not indicate publication bias (p=0.83 and p=0.85, respectively). Visual inspection of the funnel plot demonstrated an approximately symmetrical distribution of the inverse variances, which is consistent with these findings (Appendix page 13).

Discussion

Results from this comprehensive meta-analysis of RCTs with at least 1 year of follow-up indicate low-fat dietary interventions do not lead to greater weight loss when compared with higher fat dietary interventions of similar intensity, regardless of the weight loss intention of the trial. In fact, in the setting of weight loss trials, higher fat, low-carbohydrate dietary interventions led to a modest but significant greater long-term weight loss than low-fat interventions. Other higher fat dietary interventions led to similar weight loss as the low-fat groups, whether the trial had a weight loss goal or not. Low-fat interventions were favored only in comparison with interventions of lesser intensity, particularly those in which controls were only asked to maintain their usual diet. Furthermore, trials achieving greater differences in dietary fat intake and serum triglyceride concentrations resulted in greater weight loss under the higher fat interventions. Although these are not perfect measures of dietary fat intake, given the potential for measurement error in self-reported diet and confounding by weight loss for triglycerides as a marker of fat intake, results were consistent between these two methods.

This systematic literature review and meta-analysis highlights several important points. First, of the 53 eligible RCTs, 19 included higher fat comparator groups which maintained their usual intake, while the low-fat groups underwent interventions with more frequent and/or more intense interaction with research staff. Such comparisons do not provide evidence to support the effect of the low-fat diets themselves, since the effect of lowering total fat intake cannot be distinguished from the other components of the intervention. Stratifying by this type of comparator group (Figure 2), it is clear that lowering fat intake was not an independent contributor to weight loss. Second, despite concerted efforts among motivated clinical trial participants and staff, the average weight loss in all groups after a median 1 year of follow-up was a modest 2.7 kg, and 3.8 kg when calculated among weight loss trials only.

Our findings contrast with the findings of a previous systematic review and meta-analysis, which concluded that reduction in total fat intake leads to clinically meaningful weight loss, reporting 1.57 kg (95% CI=1.97 to 1.16) greater weight loss for low-fat vs. other diet interventions.(33) The main differences in their study selection criteria from ours were their inclusion of trials with <1 year of follow-up and their deliberate exclusion of trials with any weight loss intention. Trials of short duration (e.g. 6 months) are unlikely to demonstrate effects representative of long-term effects of diet on weight. Additionally, evaluating low-fat diets for weight loss exclusively among trials without a weight loss goal excluded a substantial proportion of the available literature, giving a pooled estimate that was over-weighted by trials comparing low-fat with "usual diet", as well as trials conducted among populations at high risk for specific non-body weight related endpoints of interest (e.g., cholesterol-lowering, breast cancer prevention, etc). In our current meta-analysis among trials without a weight loss goal and at least 1 year duration, we found that after removing comparisons between low-fat and "usual diet", low-fat interventions did not lead to greater weight loss that higher fat interventions (n=7; WMD=0.26 kg, 95% CI=-0.39 to 0.91). In fact, of the 33 trials included in their overall analysis, only 8 comparisons were conducted among trials giving similar attention to the low-fat and comparator treatment arms, and only 1 of these lasted at least 1 year. Furthermore, only 3 were among healthy participants. Therefore, generalizability of their findings to overall populations intending to lose weight is highly questionable, and their estimated effects of reducing fat intake are likely to be seriously confounded by differences in comparator group intensity, which was demonstrated to be a major source of heterogeneity in our analysis.

Johnston, et al, conducted a *network* meta-analysis among trials comparing named popular diet programs.(34) Pooling both direct (i.e., head-to-head comparison of two interventions within a single RCT) and indirect comparison (i.e., non-randomized comparisons of two intervention effects derived from separate trials) produced estimates similar to ours, indicating significant weight loss at 12 months for low-fat interventions compared with "usual diet", and no significant benefit when compared with other dietary interventions of similar intensity. Limitations of indirect comparisons, however, include the inability to control for between-study and between-participant differences that may confound the pooled estimates. Another recent meta-analysis evaluated 13 trials of low-fat vs. very low-carbohydrate diet interventions with at least 12 months of follow-up.(35) Their pooled estimate indicated a 0.91 kg (95% CI=1.65 to 0.17) greater weight loss for very low-carbohydrate compared with low-fat diet interventions, consistent with our pooled estimate of 1.15 kg for low-carbohydrate vs. low-fat weight loss interventions.

A limitation of this meta-analysis is the substantial heterogeneity within several strata, indicating inconsistent effects across studies. Heterogeneity to some degree would be expected given the various intervention designs, baseline characteristics of the participants, and comparator diets. Stratified analyses reduced heterogeneity in many cases. Additionally, our manuscript did not have a pre-published protocol, and our search was limited to English language publications, did not include other potential databases, or a search of grey literature, which may have missed trials. Finally, the majority of RCTs of ≥1 year duration were not feeding trials, since large-scale long-term trials of this nature can be costly; therefore, our analysis addresses the effectiveness of dietary interventions, and not necessarily the diets themselves.

The strength of evidence of the literature included in this systematic review is variable with a high concern for attrition bias from significant drop-out and loss-to-follow-up rates in the majority of trials. Retaining participants for long-term lifestyle interventions can be difficult and bias is a concern when attrition is related to intervention assignment. Other bias measures were difficult to assess as a whole, without details of methods for randomization and allocation concealment, and whether staff members measuring outcomes were blinded.

Findings from our systematic literature review and meta-analysis of RCTs fail to support the efficacy of low-fat diet interventions over higher fat diet interventions of similar intensity for significant long-term clinically meaningful weight control. Previous trials comparing low-fat diet interventions with "usual diet" or minimal intensity control groups have mislead perceptions of the efficacy of reductions in fat intake as a strategy for long-term weight loss. In fact, comparisons of similar intervention intensity conclude that dietary interventions lower in total fat intake lead to significantly less weight loss compared with higher fat, low-carbohydrate diets. Health and nutrition guidelines should cease recommending low-fat diets for weight loss given the clear lack of long-term efficacy over other similar intensity dietary interventions. Additional research is needed to identify optimal intervention strategies for long-term weight loss and weight maintenance, including the need to look beyond variations in macronutrient composition.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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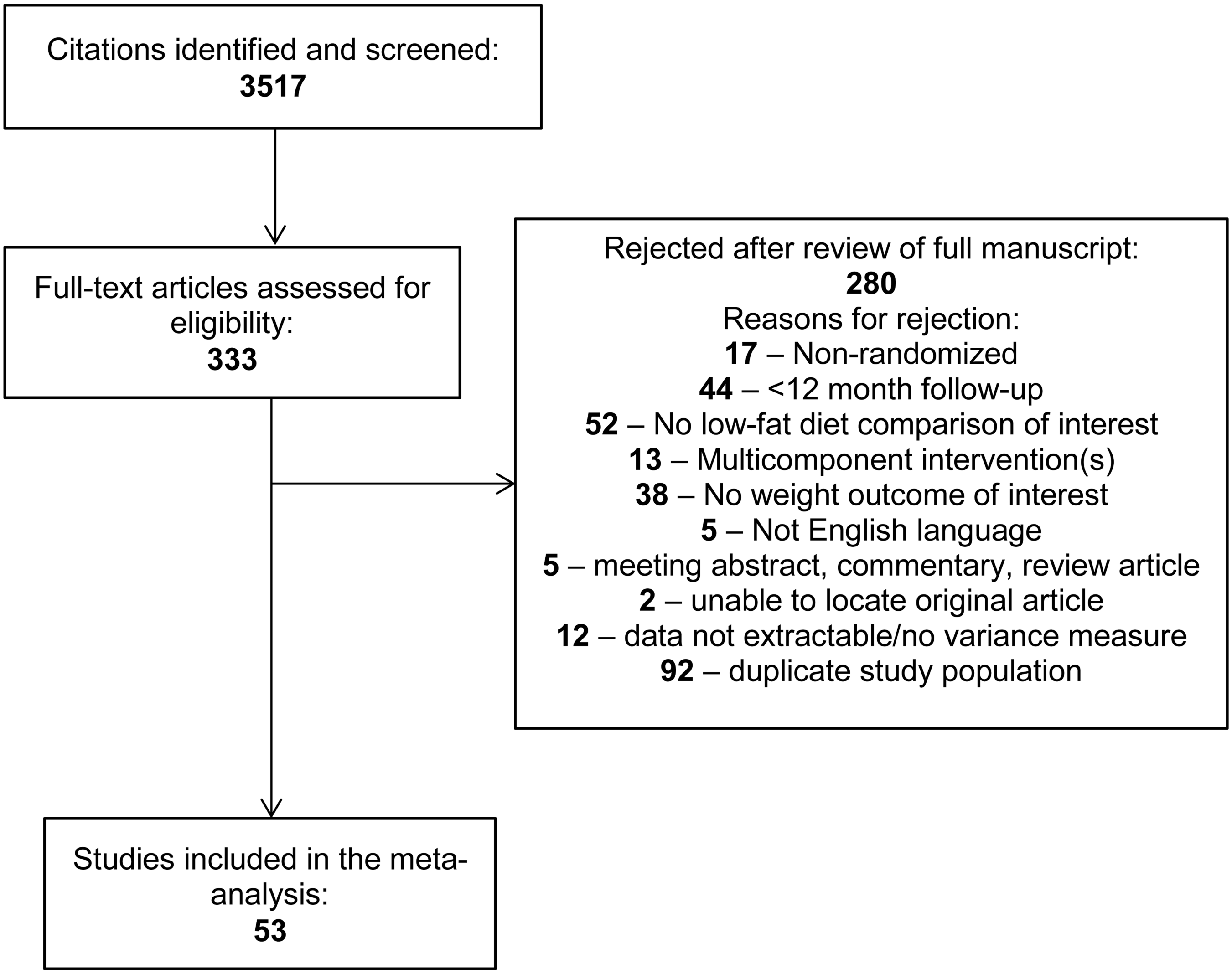

Figure 1.
PRISMA Flow Diagram

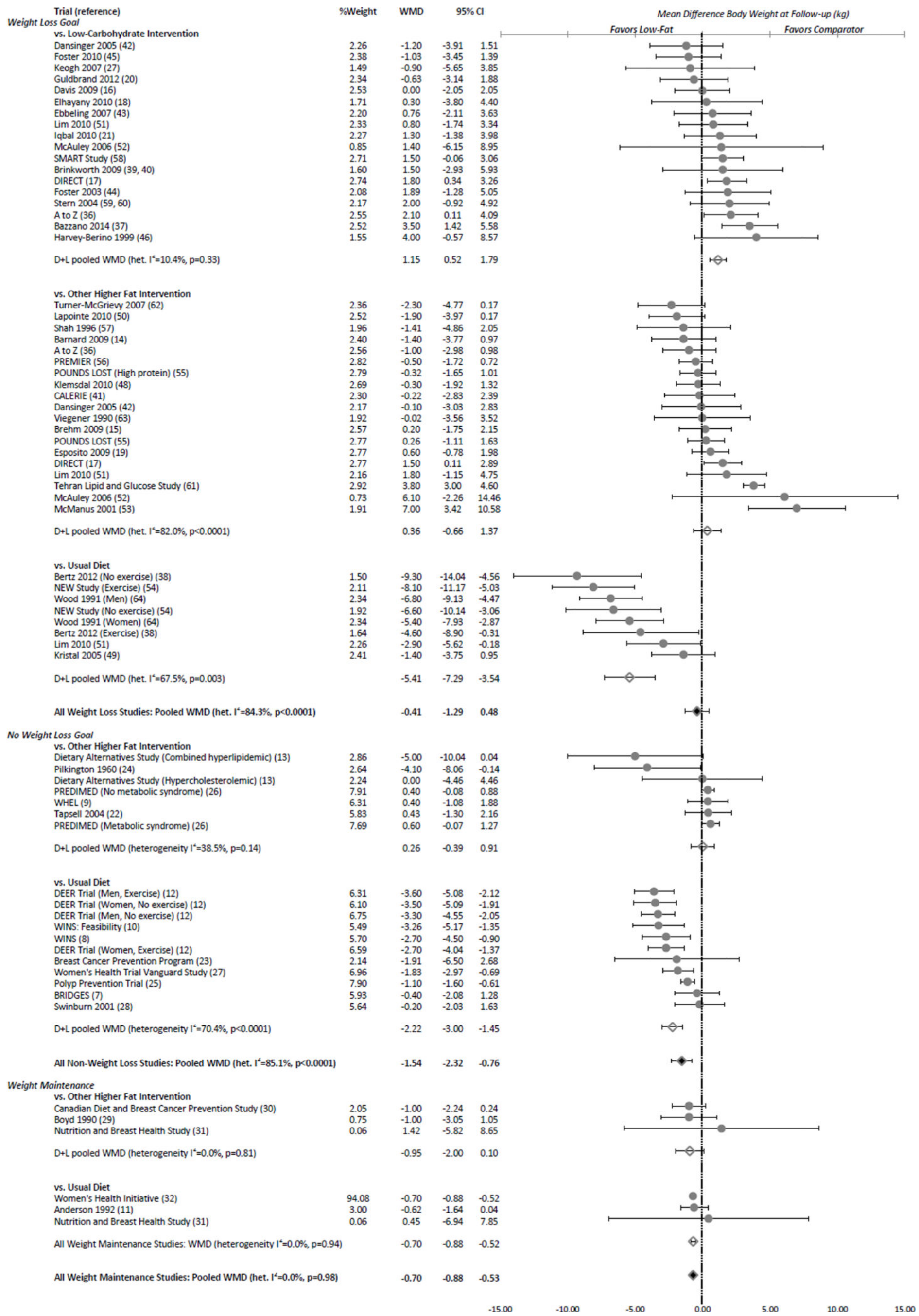

Figure 2.

Random effects pooled weighted mean difference (kg) for low-fat vs. comparator dietary interventions from 53 randomized trials reporting at least 1 year of follow-up, by weight loss intention and comparator intervention.

Table 1

Randomized trials of low-fat versus other dietary interventions of at least 1 year duration among adults, included in the meta-analysis.

Trial Name	N randomized; Population	Country	Weight loss goal	Low-fat diet(s) intervention	Comparator diet(s) intervention	Follow-up duration (years)
A to Z (36)	311; Overweight, premenopausal women	US	Yes	[1] LEARN (*reduced calorie*); [2] Ornish (<10% fat; *reduced calorie*)	[1] Atkins low-carbohydrate; [2] Zone (30% fat; *reduced calorie*)	1
Anderson 1992 (11)	117; Moderate hypercholesterolemia	US	Maintain	American Heart Association Phase II (25% fat)	Usual diet	1
Barnard 2009 (14)	99; Type 2 diabetes	US	Yes	Vegan (10% fat)	American Diabetes Association Diet 2003 (30% fat; *reduced calorie*)	1.4
Bazzano 2014 (37)	148; Obese	US	Yes	National Cholesterol Education Program (<30% fat)	Low carbohydrate	1
Bertz 2012 (38)	68; Breastfeeding mothers	Sweden	Yes	Nordic Nutrition Guidelines (<30% fat; *reduced calorie*)	Usual diet	1
Boyd 1990 (29)	295; Women at high breast cancer risk	Canada	Maintain	15% fat	Canadian Food Guide (No fat intake advice)	1
Breast Cancer Prevention Program (23)	194; Women at high breast cancer risk	US	No	15% fat	Usual diet	1
Brehm 2009 (15)	124; Overweight/obese with type 2 diabetes	US	Yes	High carbohydrate (25% fat; *reduced calorie*)	High mono-unsaturated fat (40% fat; *reduced calorie*)	1
BRIDGES (7)	172; Women with recent breast cancer	US	No	Nutrition Education Program (20% fat)	Usual diet	1
Brinkworth 2009 (39, 40)	118; At risk for metabolic syndrome	Australia	Yes	30% fat (*reduced calorie*)	Atkins low-carbohydrate (61% fat; *reduced calorie*)	1
CALERIE Phase I (41)	34; Overweight	US	Yes	High glycemic index, food provided (20% fat; *reduced calorie*)	Low glycemic index, food provided (30% fat; *reduced calorie*)	1
Canadian Diet and Breast Cancer Prevention Study (30)	4690; Women at high breast cancer risk	Canada	Maintain	15% fat	Canadian Food Guide (No fat intake advice)	10
Dansinger 2005 (42)	160; At risk for cardiovascular disease	US	Yes	Ornish (<10% fat)	[1] Atkins low-carbohydrate; [2] Zone (30% fat); [3] Weight Watchers (*reduced*	1

Trial Name	N randomized; Population	Country	Weight loss goal	Low-fat diet(s) intervention	Comparator diet(s) intervention	Follow-up duration (years)
					calorie)	
Davis 2009 (16)	105; Type 2 diabetes	US	Yes	Diabetes Prevention Program diet (25% fat)	Atkins low-carbohydrate	1
DEER (12)	377; Hypercholesterolemia	US	No	National Cholesterol Education Program (<30% fat)	Usual diet	1
The Dietary Alternatives Study (13)	508; Men with hypercholesterolemia	US	No	[1] 26% fat; [2] 22% fat; [3] 18% fat	30% fat	1
DIRECT (17)	322; Type 2 diabetes, cardiovascular disease, or obese	Israel	Yes	American Heart Association (30% fat; *reduced calorie*)	[1] Mediterranean diet (35% fat; *reduced calorie*); [2] Atkins low-carbohydrate	2
Ebbeling 2007 (43)	73; Obese young adults	US	Yes	20% fat	Low glycemic-index carbohydrates (35% fat)	1.5
Elhayany 2010 (18)	259; Type 2 diabetes	Israel	Yes	[1] American Diabetes Association 2003 (30% fat; *reduced calorie*); [2] Low-fat Mediterranean (30% fat; *reduced calorie*)	Low carbohydrate Mediterranean diet (45% fat; *reduced calorie*)	1
Esposito 2009 (19)	215; Type 2 diabetes	Italy	Yes	American Heart Association 2000 (<30% fat; *reduced calorie*)	Mediterranean diet (>30% fat; *reduced calorie*)	4
Foster 2003 (44)	63; Obese	US	Yes	25% fat (*reduced calorie*)	Atkins low-carbohydrate	1
Foster 2010 (45)	307; Obese	US	Yes	30% fat (*reduced calorie*)	Atkins low-carbohydrate	2
Guldbrand 2012 (20)	61; Type 2 diabetes	Sweden	Yes	<30% fat (*reduced calorie*)	Low-carbohydrate (50% fat; *reduced calorie*)	2
Harvey-Berino 1999 (46)	80; Overweight/obese	US	Yes	20% fat	Low-calorie	1.5
Iqbal 2010 (21)	144; Type 2 diabetes, obese	US	Yes	<30% fat (*reduced calorie*)	Low-carbohydrate	2
Keogh 2007 (47)	44; Overweight/obese	Australia	Yes	20% fat (*reduced calorie*)	Low-carbohydrate (27% fat; *reduced calorie*)	1
Klemsdal 2010 (48)	202; Metabolic syndrome	Norway	Yes	30% fat (*reduced calorie*)	Low glycemic load (35–40% fat; *reduced calorie*)	1

Trial Name	N randomized; Population	Country	Weight loss goal	Low-fat diet(s) intervention	Comparator diet(s) intervention	Follow-up duration (years)
Kristal 2005 (49)	93; Overweight/obese with esophageal metaplasia	US	Yes	20% fat (*reduced calorie*)	Usual diet	3
Lapointe 2010 (50)	68; Overweight/obese postmenopausal women	Canada	Yes	Reduce fat intake	Increase fruits and vegetables	1.5
Lim 2010 (51)	113; High cardiovascular disease risk	Australia	Yes	Food provided (10% fat; *reduced calorie*)	[1] Low-carbohydrate, food provided (60% fat; *reduced calorie*); [2] High unsaturated fat, food provided (30% fat; *reduced calorie*); [3] Usual diet	1.25
McAuley 2006 (52)	96; Women overweight/obese with insulin resistance	New Zealand	Yes	Diabetes and Nutrition Study Group of the European Association for the Study of Diabetes (<30% fat)	[1] low carbohydrate Atkins diet; [2] Zone diet (30% fat)	1
McManus 2001 (53)	101; Overweight	US	Yes	20% fat (*reduced calorie*)	35% fat (*reduced calorie*)	1.5
Nutrition and Exercise in Women Study (54)	439; Postmenopausal overweight/obese women	US	Yes	<30% fat (*reduced calorie*)	Usual diet	1
Nutrition and Breast Health Study (31)	122; Premenopausal women at risk of breast cancer	US	Maintain	(1) 15% fat; (2) High fruits and vegetables (15% fat)	(1) Usual diet; (2) High fruits and vegetables	1
Pilkington 1960 (24)	58; Men with ischemic heart disease	UK	No	20 g fat/day	Increase unsaturated fats	1.5
Polyp Prevention Trial (25)	2079; Recent colorectal adenoma	US	No	20% fat	Usual diet	3.1
Pounds Lost Trial (55)	811; Overweight/obese	US	Yes	[1] 20% fat (*reduced calorie*); [2] high protein (20% fat; *reduced calorie*)	[1] 40% fat (*reduced calorie*); [2] high protein (40% fat; *reduced calorie*)	2
PREDIMED (26)	7447; High cardiovascular disease risk	Spain	No	Reduce fat intake	Mediterranean Diet + [1] increase extra-virgin olive oil intake, [2] mixed nuts intake	4.8
PREMIER (56)	810; Prehypertension	US	Yes	DASH (<25% fat; *reduced*	30% fat (*reduced calorie*)	1.5

Trial Name	N randomized; Population	Country	Weight loss goal	Low-fat diet(s) intervention	Comparator diet(s) intervention	Follow-up duration (years)
				calorie)		
Shah 1996 (57)	122; Obese women	US	Yes	20 g fat/day	30% fat (*reduced calorie*)	1
SMART Study (58)	200; Overweight/obese	Germany	Yes	German Nutrition Society (30% fat; *reduced calorie*)	Low-carbohydrate (35% fat; *reduced calorie*)	1
Stern 2004 (59, 60)	132; Morbidly obese	US	Yes	NHLBI (30% fat; *reduced calorie*)	Low-carbohydrate	1
Swinburn 2001 (28)	176; Glucose intolerance	New Zealand	No	Reduce fat	Usual diet	5
Tapsell 2004 (22)	63; Type 2 diabetes	Australia	No	27% fat	37% fat	1
Tehran Lipid and Glucose Study (61)	100; Overweight/obese	Iran	Yes	20% fat (*reduced calorie*)	30% fat (*reduced calorie*)	1.2
Turner-McGrievy 2007 (62)	64; Overweight/obese postmenopausal women	US	Yes	Vegan (10% fat)	National Cholesterol Education Program (<30% fat)	2
Viegener 1990 (63)	85; Overweight/obese women	US	Yes	15–25% fat (*reduced calorie*)	30% fat (*reduced calorie*)	1
Women's Health Initiative Dietary Modification Trial (32)	48835; Postmenopausal women	US	Maintain	20% fat	Usual diet	7.5
Women's Health Trial Vanguard Study (27)	303; Women at high breast cancer risk	US	No	20% fat	Usual diet	2
Women's Healthy Eating and Living (WHEL) (9)	3088; Women with previous breast cancer	US	No	15–20% fat	USDA guidelines (<30% fat)	7.3
Women's Intervention Nutrition Study (WINS) (8)	2437; Women with breast cancer	US	No	15% fat	General counseling on nutritional adequacy	5

Trial Name	**N randomized; Population**	**Country**	**Weight loss goal**	**Low-fat diet(s) intervention**	**Comparator diet(s) intervention**	**Follow-up duration (years)**
Women's Intervention Nutrition Study (WINS) Feasibility (10)	290; Women with postmenopausal breast cancer	US	No	20% fat	General counseling on nutritional adequacy	1.5
Wood 1991 (64)	294; Overweight/obese	US	Yes	National Cholesterol Education Program (<30% fat; *reduced calorie*)	Usual diet	1

Table 2

Random effects pooled weighted mean difference (kg) for low-fat vs. comparator dietary interventions from 36 randomized weight loss trials reporting at least 1 year of follow-up, stratified by trial characteristics.

	N Comparisons	WMD (95% CI)	p-value	I^2 (p-value for heterogeneity)
Weight Loss Goal				
Similar Intervention Intensity	33	0.62 (−0.08, 1.32)	0.084	71.6% (p<0.0001)
Comparator Diet				
Low-Carbohydrate	18	1.15 (0.52, 1.79)	<0.001	10.4% (p=0.33)
Other Higher Fat Intervention	19	0.36 (−0.66, 1.37)	0.49	82.0% (p<0.0001)
Usual Diet	0	--		--
Caloric Restriction				
Both Interventions	18	0.74 (−0.19, 1.68)	0.12	78.4% (p <0.0001)
Neither Intervention	8	0.33 (−1.18, 1.83)	0.67	65.1% (p=0.005)
Low-Fat Only	6	1.49 (0.53, 2.45)	0.002	7.7% (p=0.37)
Comparator Only	5	−0.62 (−1.95, 0.72)	0.37	15.5% (p=0.32)
Chronic Disease Population				
No	25	0.77 (−0.15, 1.69)	0.10	76.1% (p <0.0001)
Yes	8	0.37 (−0.33, 1.07)	0.30	10.3% (p=0.35)
Difference in Fat Intake at Follow-up (% Calories)				
<5% Difference in Fat Intake	8	0.14 (−0.80, 1.09)	0.77	30.1% (p=0.19)
≥5% Difference in Fat Intake	18	1.04 (0.06, 2.03)	0.038	77.7% (p<0.0001)
Difference in Triglycerides at Follow-up (mg/dL Change)				
<5 mg/dL Change Difference	8	−0.21 (−0.86, 0.43)	0.52	0.0% (p =0.92)
≥5 mg/dL Greater Change in Low-Fat Group	17	1.38 (0.50, 2.25)	0.002	62.3% (p<0.0001)
No Weight Loss Goal				
Similar Intervention Intensity	4	−1.71 (−4.52, 1.10)	0.23	59.3% (p=0.061)
Comparator Diet				
Low-Carbohydrate	0	--	--	--
Other Higher Fat Intervention	4	−1.71 (−4.52, 1.10)	0.23	59.3% (p=0.061)
Usual Diet	0	--		--
Caloric Restriction				
Both Interventions	0	--		--
Neither Intervention	2	−1.47 (−5.85, 2.91)	0.51	76.3% (p=0.04)
Low-Fat Only	0	--		--
Comparator Only	0	--		--
Chronic Disease Population				
No	0	--		--
Yes	4	−1.71 (−4.52, 1.10)	0.23	59.3% (p=0.061)
Difference in Fat Intake at Follow-up (% Calories)				
<5% Difference in Fat Intake	1	NA	NA	NA
≥5% Difference in Fat Intake	2	−2.18 (−6.19, 1.83)	0.29	45.0% (p=0.18)

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	N Comparisons	WMD (95% CI)	p-value	I^2 (p-value for heterogeneity)
Difference in Triglycerides at Follow-up (mg/dL Change)				
<5 mg/dL Change Difference	1	NA	NA	NA
≥5 mg/dL Greater Change in Low-Fat Group	1	NA	NA	NA

WMD=DerSimonian and Laird random effects weighted mean difference, in kg; Negative value favors low-fat dietary intervention; Positive value favors higher fat comparator intervention